HELLER EHRMAN WHITE & MCAULIFFE LLP Sheet 1 of 8 Title: METHODS FOR THE PRODUCTION OF MULTIMERIC PROTEINS, AND RELATED COMPOSITIONS Docket No.: 38814-351B, Gijs van Rooijen Filed: December 19, 2001

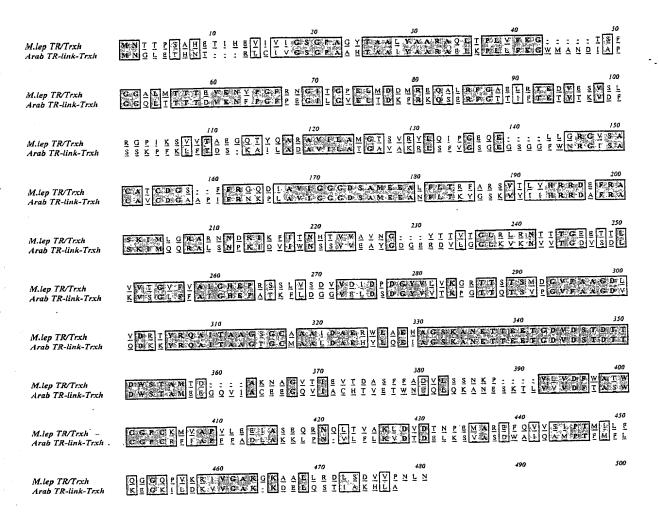
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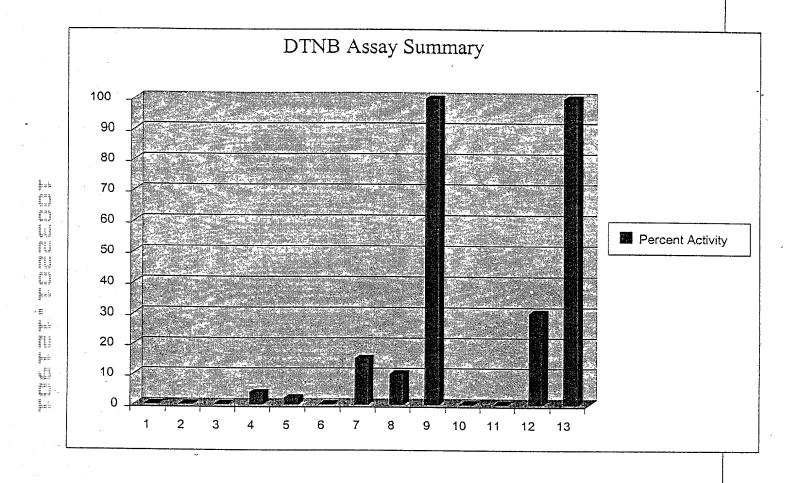
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HETEROMULTIMERS

Class	Heteromultimer	Example sequence reference for
		heteromultimeric subunits
Biosynthetic	3-methyl-2-oxobutanoate	McKean, et al. Biochim. Biophys. Acta (1992)
	dehydrogenase (2-oxoisovalerate	1171:109-112 / Chuang, J.L., et al. FEBS Lett. a
	dehydrogenase (lipoamide))- E1	(1990) 262 (2), 305-309.
	component)	
Biosynthetic	3-oxoadipate CoA-transferase	Parales, R.E. and Harwood, S.C. J. Bacteriol. (1992)
		174:4657-4666
Biosynthetic	anthranilate synthase:indole-3-glycerol	Zalkin, H.; et al. J. Biol. Chem. (1984) 259:3985-
	phosphate synthase	3992 .
Biosynthetic	beta-ketoacyl-[acyl carrier protein]	Siggaard-Andersen, M. et al. Proc. Natl. Acad. Sci.
	synthase I	U.S.A. (1991) 88:4114-4118
Biosynthetic	butyrateacetoacetate CoA-transferase	Fischer, R.J., et al. J. Bacteriol. (1993) 175 (21),
		6959-6969.
Biosynthetic	cAMP dependent protein kinase	Mutzel, R et al. Proc. Natl. Acad. Sci. U.S.A. (1987)
		84:6-10./ Burki, E., et al. Gene (1991) 102 (1), 57-
		65.
Biosynthetic	carbamoyl-phosphate synthase	Shigenobu, S., et al. Nature. (2000) 407 (6800), 81-
		86.
Biosynthetic	Creatine kinase	Billadello, J.J.; et al. Biochem. Biophys. Res.
		Commun. (1986) 138:392-398. / Roman, D.; et al.
		Proc. Natl. Acad. Sci. U.S.A. (1985) 82:8394-8398.
Biosynthetic	gamma-glutamyltransferase (gamma-	Papandrikopoulou, A.; et al. Eur. J. Biochem.
	glutamyl transpeptidase)	(1989) 183:693-698.
Biosynthetic	glutathione transferase	Morrow, C.S. et al. Gene (1989) 75:3-11
Biosynthetic	glycerol-3-phosphate dehydrogenase	Cole, S.T. et al. J. Bacteriol. (1988) 170:2448-2456.
Biosynthetic	guanylate cyclase	Hinsch, K.D. et al. FEBS Lett. (1988) 239:29-34/
		Koesling, D. et al. FEBS Lett. (1990) 266:128-132.
Biosynthetic	heterodisulfide reductase	Smith, D.R., et al. J. Bacteriol. (1997) 179 (22),
		7135-7155.
Biosynthetic	human cathepsin	Ritonja, A. et al. FEBS Lett. (1988) 228:341-345.
Biosynthetic	Hydrogenase	Menon, N.K. et al. J. Bacteriol. (1990) 172:1969-
		1977.
Biosynthetic	Meprin A	Johnson, G.D. and Hersh, L.B. J. Biol. Chem.
		(1992) 267:13505-13512.
Biosynthetic	methionine adenosyltransferase	Horikawa, S.; Tsukada, K. FEBS Lett. (1992)
		312:37-41.
Biosynthetic	methylmalonyl-CoA mutase	Jackson, C.A. et al. Gene (1995) 167:127-132.
Biosynthetic	mitochondrial processing peptidase	Pollock, R.A. et al. EMBO J. (1988) 7:3493-3500.
Biosynthetic	Na+/K+-exchanging ATPase	Shull, G.E., et al. Biochemistry (1986) 25 (25),
		8125-8132./Mercer,R.W., et al.
		Mol. Cell. Biol. (1986) 6 (11), 3884-3890./
		Mercer, R.W., et al. J. Cell Biol. (1993) 121 (3),
		579-586.
Biosynthetic	NAD(+)-dependent isocitrate	Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem.
	dehydrogenase	(1992) 267:16417-16423. /Cupp, J.R. and
		McAlister-Henn, L.
-		J. Biol. Chem. (1991) 266:22199-22205.
Biosynthetic	phosphoribosylformylglycinamidine	Ebbole, D.J.; Zalkin, H. J. Biol. Chem. (1987)
	synthase	262:8274-8287.
Biosynthetic	protocatechuate 3,4-dioxygenase	Frazee, R.W.; et al. J. Bacteriol. (1993) 175:6194-
		6202.
Biosynthetic	S-100 protein	Engelkamp, D.; et al. Biochemistry (1992)



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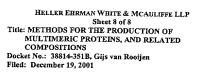
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		31:10258-10264. / Allore, R.J.; et al. J. Biol. Shem.
Direct de d		(1990) 265:15537-15543.
Biosynthetic	sucrosefructan 6-fructosyltransferase	Sprenger, N.; <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1995) 92:11652-11656.
Biosynthetic	Superoxide dismutase	Capo, C.R.; et al. Biochem. Biophys. Res. Commun. (1990) 173:1186-1193.
Biosynthetic	Urease	Labigne, A.; et al. J. Bacteriol. (1991) 173:1920-1931.
Biosynthetic	urokinase-type plasminogen activator (urokinase)	Belin, D. et al. Eur. J. Biochem. (1985) 148:225-232.
Biosythetic	methylmalonyl-coenzyme A mutase	Birch, A., et al J. Bacteriol. (1993) 175 (11), 3511-3519.
Calcium binding	Calcineurin	Muramatsu, T. and Kincaid, R.L. Biochim. Biophys. Acta (1993) 1178 (1), 117-120 / Guerini, D. et al. DNA (1989) 8:675-682.
Calcium binding	Calgranulin	Imamichi, T. <i>et al.</i> Biochem. Biophys. Res. Commun. (1993) 194:819-825.
Calcium binding	Calpain	Aoki, K. et al. FEBS Lett. (1986) 205:313-317.
DNA binding	AP1	van Straaten, F., et al. Proceedings of the National Academy of Sciences of the United States of America. (1983) 80 (11), 3183-3187. /Hattori, K., et al Proceedings of the National Academy of Sciences of the United States of America. (1988) 85 (23), 9148-9152.
DNA binding	сМус-Мах	Schreiber-Agus, N et al. Mol. Cell. Biol. (1993) 13 (5), 2765-2775.
DNA binding	DNA binding protein HU-1/HU-2	Laine, B. et al. Eur. J. Biochem. (1980) 103:447-461.
DNA binding	hepatic nuclear factor 1	Bach, I. et al. Nucleic Acids Res. (1992) 20 (16), 4199-4204. / Rey-Campos, J. et al. EMBO J. (1991) 10 (6), 1445-1457.
DNA binding	Integration host factor	Miller, H.I. Cold Spring Harbor symposia on quantitative biology. (1984) 49, 691-698. / Flamm, E. and Weisberg, R.A. J. Mol. Biol. (1985) 183:117-128.
DNA binding	Ku	Reeves, W.H. and Sthoeger, Z.M. J. Biol. Chem.
		(1989) 264 (9), 5047-5052. / J. Biol. Chem. (1989) 264 (23), 13407-13411.
DNA binding	MutS	Bocker et al. 1999. Cancer Research 59, 816-822.
DNA binding	NF-E2	Chan, J. Y. et al Proc. Natl. Acad. Sci. U.S.A. (1993) 90 (23), 11366-11370./ Toki, T., et al. Oncogene (1997) 14 (16), 1901-1910.
DNA binding	nuclear factor kB (NFkB)	Kieran M, et al. Cell. (1990) Sep 7;62(5):1007-18./ Ruben SM, et al. Science (1991) Mar 22;251(5000):1490-3. Erratum in: Science (1991) Oct 4;254(5028):11
Electron transport	corrinoid/iron-sulfur protein	Lu, W.P. et al. J. Biol. Chem. (1993) 268:5605- 5614.
Electron transport	cytochrome d ubiquinol oxidase	Green, G.N. et al. J. Biol. Chem. (1988) 263:13138-13143.
Electron transport	cytochrome-c3 hydrogenase	Menon, N.K. et al. J. Bacteriol. (1987) 169:5401-5407.
Electron transport	electron transfer flavoprotein	Finocchiaro, G. et al. Biol. Chem. (1988) 263:15773-15780. / Finocchiaro, G. et al. Eur. J.

Biochem. (1993) 213:1003-1008.



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Electron transport	xylene monooxygenase	Chay, ID and Harryana C. E., I Disale
Licetion transport	xylene monooxygenase	Shaw, J.P. and Harayama, S. Eur. J. Biochem.
		(1992) 209:51-61. / Kasai, Y., et al. J. Bacteriol.
Growth factor	handtautta grouth factor	(2001) 183 (22), 6662-6666.
Growth factor	hepatocyte growth factor human chorionic gonadotropin	Nakamura, T. et al. Nature (1989) 342:440-443.
		Morgan, F.J. et al. J. Biol. Chem. (1975) 250 (13), 5247-5258.
Growth factor	Platelet-derived growth factor	Takimoto, Y., et al. Hiroshima J. Med. Sci. (1993)
†		42 (1), 47-52./ Josephs, S.F., et al. Science (1984)
	•	225 (4662), 636-639.
Hormone	Bombyxin	Adachi, T. et al. J. Biol. Chem. (1989) 264:7681-7685.
Hormone	Follicle stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.
		Genet. (1981) 1 (1), 3-18. / Watkins, P.C., et al. DNA (1987) 6 (3), 205-212.
Hormone	Insulin	Bell, G.I., Pictet, R.L., Rutter, W.J., Cordell, B.,
Tiomione	Insuin	Tischer, E. and Goodman, H.M.
·		Sequence of the human insulin gene. Nature. 284
·		(5751), 26-32 (1980)
		(3731), 20-32 (1980)
Hormone	Luteinizing Hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.
	Editinizing Homone	Genet. (1981) 1 (1), 3-18. / Shome,B. and
		Parlow, A.F. J. Clin. Endocrinol. Metab. (1973) 36
		(3), 618-621.
Hormone	Thyroid stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.
		Genet. (1981) 1 (1), 3-18. / Hayashizaki Y, et al.
		FEBS Lett. (1985) 188 (2), 394-400.
Immune	B-cell antigen receptor complex	Hashimoto, S. et al. J. Immunol. (1993) 150 (2), 491-
	2 con uningen receptor complex	498. / Flaswinkel, H. and Reth, M.
		Immunogenetics (1992) 36 (4), 266-269.
Immune	Cell surface CD8 molecules	Ureta-Vidal, A., et al. Immunogenetics (1999) 49
		(7-8), 718-721.
Immune	human complement subcomponent Clq	Sellar, G.C. et al. Biochem. J. (1991) 274:481-490.
Immune .	T cell receptor	Talken, B.L. et al. Scand. J. Immunol. (2001) 54 (1-
	•	2), 204-210.
Photosynthesis	C-phycocyanin	Offner, G.D. et al. J. Biol. Chem. (1981) 256:12167-
	, • • • • • • • • • • • • • • • • • • •	12175. / Troxler, R.F. et al. J. Biol. Chem. (1981)
		256:12176-12184.
Photosynthesis	ferroredoxin-thioredoxin reductase	Chow, L.P. et al. Eur. J. Biochem. (1995) 231:149-
		156. / Iwadate, H. et al. Eur. J. Biochem. (1994)
		223:465-471.
Photosynthesis	Light harvesting complex I	Proc. Natl. Acad. Sci. U.S.A. (1984) 81, 189-192.
Photosynthetic	cytochrome b559	Carrillo, N. et al. Curr Genet. 1986;10(8):619-24.
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